REMARKS

Claims 1-36, 38, 39, 43, 44, and 50-62 were preciously cancelled. Claim 46 was previously withdrawn. Applicant reserve the right to file divisional and continuation applications directed towards the cancelled and withdrawn subject matter. Claims 37, 40-42, 45, 47-49, 63 and 64 are currently under consideration.

Withdrawn Rejections

Applicant acknowledges with thanks the Examiner's withdrawal of the rejection of claims 37, 40-42, 45, 47-49, 63 and 64 under 35 U.S.C. §112, first paragraph for lack of written description.

Rejection Under 35 U.S.C. §112, First Paragraph

Claims 37, 40-42, 45, 47-49, 63 and 64 are rejected under 35 U.S.C. §112, first paragraph as allegedly failing to comply with the enablement requirement.

In considering the *Wands* factor of the nature of the invention as whether the specification would require undue experimentation by one of skill in the art, the Examiner at page 9 states that the "claimed invention is directed at the treatment of diseases, wherein the elected disease is hepatitis C virus, HCV, with the administration of a glycolipid" and that "the claimed invention relates to the application of a glycolipid to regulate and manipulate immune responses, Th1 and Th2 responses, in mammalian subjects..."

With respect to the *Wands* factor of the breadth of the claims, the Examiner at page 10 states that "the claims encompass all diseases..."

Regarding the *Wands* factor of presence or absence of working examples, the Examiner at pages 10-11 states that "[t]he specification does not contain any working examples demonstrating the effective use of glycolipids to treat HCV infection" and that "Applicant has not set forth any guidance or direction relating to the immune component that must be changed or modulated in order to render treatment to HCV infected subjects."

As to the Wands factor of the state of the art, the Examiner at page 11 states that "[t]he hepatitis C virus (HCV) art clearly notes that the role of innate and antigen-nonspecific response to HCV has not yet been sufficiently characterized" and that in such absence, "the skilled artisan would not readily be able to practice the claimed invention without an undue burden of experimentation." The Examiner asserts at pages 11-12 that

several factors challenge the development of an effective treatment for HCV, including 1) the lack of an effective cell culture system; 2) "the absence of good animal models, outside of humans and chimpanzees," and 3) "the ability of HCV to evade effective immune recognition, including recognition by cytotoxic T lymphocytes (CTL) and shown and extremely high rate of viral persistence." The Examiner further asserts that the last enumerated factor "establishes that the type of experimentation that the skilled artisan would have to perform...is beyond routine experimentation, such as establishing rout of administration and treatment dosage amounts." See Office Action page 9.

Regarding the Wands factor of the quantity of experimentation necessary, the Examiner states on page 12 that "[i]n order to practice the claimed invention, the skilled artisan would have to blindly and unduly experiment with glycolipids, each immune component and determine the relationship among the glycolipids, each immune component and HCV infection."

Applicant respectfully traverses the rejection and maintain that claims 37, 40-42, 45, 47-49, 63 and 64 are fully enabled by the specification. The Examiner states that "Applicant has not taught nor demonstrated to the skilled artisan that the administration of any glycolipids treats HCV. All Applicant has demonstrated is an association between Gaucher's disease and hepatitis C virus infection." Office Action page 6. Applicant again respectfully disagrees with the Examiner's characterization of the present invention.

The present invention clearly teaches the administration of glycolipids for the treatment of HCV infection. Applicant has described discoveries that relate to the associations between HCV and Gaucher's disease. Prior to the research that culminated in the patent application, it was known that one of the hallmarks of HCV infection (and one that is shared with HBV) is the existence of autoimmune reactivity where the infection produces inflammatory responses against uninfected liver cells as well as against virally infected cells. As such, damage to the liver is believed to be mostly caused by these autoimmune responses rather than to viral pathogenicity. The present invention is based upon the discovery that patients with the high glycolipid levels characteristic of Gaucher's disease have reduced autoimmune responses generated by HCV infection, thus providing some benefits compared to normal patients. Applicant has used this information to artificially increase the amount of glycolipids in patients through the administration of exogenous glycolipids so that these patients exhibit Gaucher-like characteristics.

The Examiner states on page 4 of the Office Action that "There is no information provided in the specification regarding the specific immune parameter that a particular metabolite/glycolipid modulates and how the modulation results in treatment of HCV." It appears that the Examiner is equating "treatment" (an action) with the term "cure" (a result of an action). Administration of the glyolipid is a treatment regardless of what results take place. The purpose of the treatment (administration of glycolipids) is to modulate immune reactions as seen in the Gaucher patients as it is believed that this modulation will result in beneficial effects for the subject. As such, there is no particular immune parameter that is targeted. The beneficial effect for the subject is the alteration in immune parameters which will provide a heightened level of glycolipids. This understanding that the adjustment of glycolipids in a subject should reduce autoimmune induced inflammatory reactions caused by HCV infection is further supported by experimental evidence in a related patent application filed on September 30, 2003 (Serial No. 10/675,980, published as 20040171557 on September 2, 2004). This application describes other diseases that involve deleterious inflammatory responses and also describes how the administration of glycolipids was successful in relieving autoimmune inflammatory responses in multiple animal models (including ConA hepatitis, TNBS experimental colitis, non-alcoholic steatohepatitis and diabetes in ob/ob mice).

Thus, Applicant respectfully disagrees with the Examiner's conclusion that the present disclosure is inadequate for allowing the practice of the invention without undue experimentation. Contrary to the Examiner's assertions on page 9 of the Office Action, the claimed invention is not directed towards "all diseases." Rather, the invention is directed to "cancer, a viral infection and autoimmune disease," as recited in the current claims. While it is appropriate to use the specification to determine what applicant intends a term to mean, a positive limitation from the specification cannot be read into a claim that does not impose that limitation. An Examiner may not import into a claim limitations that are not part of the claims. See MPEP 8th ed. rev 6, § 2111.01. As mentioned above, a series of experiments were carried out after the current filing that demonstrate that the administration of glycolipids was beneficial in treating animal models of autoimmune disease and a form of cancer (melanoma).

The Examiner further states on page 10 of the Office Action that there is no guidance as to the particular immune component that must be changed or modulated "in order

to render treatment to HCV infected subjects." Applicant notes that such mechanisms are not included in the claim language. Again, the Examiner may not read limitations into the claim that are not part of the claim. The currently claimed method encompasses a treatment of the disease by the *administration of a glycolipid.* Adjustments of immune functions are not part of the claimed method as the user has no control over such effects other than the administration step itself. The details provided regarding the immune modulatory effects do not relate to the method itself, but are provided as explanations as to why beneficial results may be provided by the administration of glycolipids. In addition, the Examiner has not offered any evidence that this method will not work.

The Examiner states on page 11 of the Office Action that the skilled artisan is prevented from practicing the invention because the innate and antigen-nonspecific immune responses to HCV are not completely characterized. The lack of such knowledge does not prevent one of skill in the art from having the ability to administer glycolipids for the treatment HCV. Such knowledge constitutes post-hoc elucidations of the particular mechanisms that result from treatment with glycolipid administration.

The Examiner lists additional barriers to the development of HCV therapies on pages 11-12 of the Office Action, with emphasis on in vitro studies and animal models. A lack of in vitro studies and animal models with regard to HCV research has not eliminated development in this area. This is evidenced by the fact that clinical trials directed to treatments for HCV have been carried out in the absence of such studies. For Example, a Phase I study was carried out for oral tolerization with HCV antigens in Israeli et al., 2004 (Liver International 24; 295-307). Thus, application of a treatment may be performed despite the problems cited by the Examiner. Indeed, new methodologies have been developed even prior to the filing of the present application. For instance, an animal model system has been described that utilizes Severe Combined Immuno-Deficiency mice (SCID) and human hepatic cells implants. Examples of infection of such animals with an equally problematic virus, HBV, were described in US Patent Application No. 08/876,635, published as 20010007153 on July 5, 2001. These models were described as suitable for HCV. Other studies on this type of system for HCV infection were described in Galun et al., 1995 (J Inf Dis 172; 25-30), Schinazi et al., 1997 (Antiviral Research 34; 69-69) and Mercer et al., 2001 (Nat Med 7; 927-933). A primitive primate (Tupaia) was described in US Patent Application No.10,042,711, published as 20030150000 on August 7, 2003 as an animal model that

showed secondary immune dysfunctions derived from viral infection. Although HBV was described in the examples, HCV was also characterized as being suitable. Such animals had previously been shown to be infectable by HCV by Xie et al., 1998 (Virology 244; 513-520) and Zhao et al., 2002 (J Clin Invet 109; 221-232). As such, even though many previous efforts regarding evaluations of therapies for HCV may have required Phase I clinical trials, suitable in vitro and in vivo assays were available to the skilled artisan at the time of the present filing.

The Examiner states on page 12 of the office action that "This last point further establishes that the type of experimentation that the skilled artisan would have to perform in practicing the claimed invention is beyond routine experimentation, such as establishing the route of administration and treatment dosage amounts." The Examiner here acknowledges that "establishing the route of administration and treatment dosage amounts" are examples of routine experimentation. As such, these are the only requirements that would be needed to practice the invention. Also, the Examiner's comments regarding guidance and direction relating to immune parameters, Th1 vs. Th2 immune responses, innate vs. antigen-nonspecific immune responses and HCV's ability to evade effective immune recognition (Office Action pages 10-11), while certainly of interest to the scientist and researcher, are not relevant to the practice of the invention. These parameters are strictly related to establishing mechanisms of (1) how and why the treatment may be effective and (2) why Gaucher's patients may have a different response to HCV infection compared to normal subjects.

Given the level of skill in the art, the breadth of the claims, the presence of examples, the amount of direction or guidance presented and the quantity of experimentation necessary, claims 37, 40-42, 45, 47-49, 63 and 64 are fully enabled by the specification as filed. Applicant respectfully requests withdrawal of this rejection.

Conclusion

Applicant respectfully submits that all claims are in condition for allowance. Early notification of a favorable consideration is respectfully requested. In the event any issues remain, Applicant would appreciate the courtesy of a telephone call to their counsel at the number listed below to resolve such issues and place all claims in condition for allowance.

Respectfully submitted,

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